

REMARKS

The drawings have been amended in response to the Examiner's statement in the Notice to File Missing Parts of Nonprovisional Application ("Notice") mailed December 22, 2003. The Examiner stated in the Notice that the drawings contained excessive text and that although suitable descriptive legends may be used or required where necessary for an understanding of the drawing, they should contain as few words as possible. 37 CFR § 1.84(o). In response, the Applicants have amended Figures 1A, 1B, 4A, and 4B to comply with the drawing requirements under 37 CFR § 1.84.

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

Date

May 20, 2004

By



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Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Commissioner is hereby authorized to charge Deposit Account No. 08-1641 for any such fees; and applicant(s) hereby petition for any needed extension of time.

Annotated Marked-Up Drawings

Figure 1A shows the DNA sequence encoding MN3Vk cloned by RT-PCR and the predicted amino acid sequence. Underlined arrows indicate the PCR primer sequences. The putative CDR regions are in bold and underlined, and indicated. Nucleotide residues are numbered sequentially (right side). Kabat's Ig molecule numbering is used for amino acid residues (top of the residues).

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CAGGTCCTCAACTGCAGGAGTCTGGACCTGAGCTGAAGAAGCCTGGAGACAGTCAAGATATCTCAAGGTTCTGGGTATACCTTCAGA
100
GTCAGGTTGACGTCCTCAGACCTGGACTCGACTTCTTCCGACCTCTCTGTGACCTCTATAGGACGTTCCGAAGACCATATGGAAGTCT
110
Q V Q L Q E S G P E L K K P G E T V K I S C K A S G Y T F R
20
AACTATGAATGAACTGGTGAACAGGCTCCAGGAAGGTTAAAGTGGATGGCTGGATTAACACCTACCTGAGAGCCAAACATAT
180
TTGATACCTTACTTGACCCACTTGTCCGAGGTCCTTCCCAAAATTCACCTACCCGACCTATTGTGGATGTGACCTCTCGGTTGTATA
50
N Y G M N W V K Q A P G K G L K W M G W I N T Y T G E P T Y
40
CDR1
GCTGATGACTTCAAGGACGGTTTGCTTCTTTGGAAACCTCTGCCAGCACTGCCTATTTCGAGATCAACACGTCACAAATGAGGAC
270
CGACTACTGAAGTTCCTCCCAACGGAAGAGAAACCTTTGGAGACGGTCGTGACGGATAAAGCTCTAGTTGTTGCAGTTTCTTACTCCTG
80
A D D F K G R F A F S L E T S A S T A Y L Q I N N V K N E D
82A B C
ACGGCTACATATTTCTGTGCAAGAAGGATGGATGGATTCAACGGTAGCTCGACTACTGGGCCAAGGACCAAGGTCACCGTC
360
TGCCGATGTATAAAGACACAGTCTTCTCCCTACCTACCTAAAGTTGCCATCATCGGAGCTGATGACCCCGGTTCCCTGGTCCCGAGTGGCAG
90
T A T Y F C A R K G W M D F N G S S L D Y W G Q G T T V T V
100 A B C D E
110
CDR3
TCCTCA
-----
AGAGT
113
S S
366
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Figure 1B shows the DNA sequence encoding MN3VH cloned by RT-PCR and the predicted amino acid sequence. Underlined arrows indicate the PCR primer sequences. The putative CDR regions are in bold and underlined, and indicated. Nucleotide residues are numbered sequentially (right side). Kabat's Ig molecule numbering is used for amino acid residues (top of the residues).

| | | | | | |
|--------|-------------------------|---------------|----------|--------------|----|
| | 1 | 10 | 20 | 27 A B C D E | 30 |
| REIVk | DIQMTQSPSSLSASVGDRVTITC | QASQ----- | DIIKYLNW | | |
| MN3Vk | SIVM••T•L•PV•L•QAS•S•S• | SIVHSNGNT••E• | | | |
| hMN3Vk | DIQL••••••••••••••S•S• | SIVHSNGNT••E• | | | |

| | | | | |
|--------|-----------------------|---------------------|------------|----|
| | 40 | 50 | 60 | 70 |
| REIVk | YQQTGKAPKLLIYEASN | LQAGVPSRFS | SGSGTDYFTI | |
| MN3Vk | •L•K••QS•N••••KV••RFS | ••D••••••••F•LK• | | |
| hMN3Vk | ••K••••••••••KVS | NRFS••D••••••••F••• | | |

| | | | | |
|--------|--------------------------------|------------|-----------|-----|
| | 80 | 90 | 100 | 108 |
| REIVk | SSLQPEDATYYC | QQYQSLPYTF | GGTKVQITR | |
| MN3Vk | •RVEA••GV•••F•GSHV•P••G••LEIKR | | | |
| hMN3Vk | ••••••••••F•GSHV•P••G••EIKR | | | |

Figure 4A. Amino acid sequence alignment of REI, MN3 and hMN3 light chain variable domains. Dots indicate the residues in MN3 is identical to the corresponding residues in REI. Dashes represent gaps introduced to aid the alignment. Boxed represent the CDR regions. Both N- and C-terminal residues (underlined) of hMN3 are fixed by the staging vector used. Therefore, the corresponding terminal residues of MN3 are not compared with that of REI. Kabat's Ig molecule numbering scheme is used (same as in Fig. 1A).

| | | | | | | | | |
|--------|-----|-------------------------------|-----|-----|-----|----|----|-------|
| EU_VH | 1 | PVQLVQSGAEVKKPGSSVKVSKASGGTFS | 20 | RS | 30 | AI | 40 | WVRQA |
| MN3VH | | QVQLQE | 10 | P | 20 | L | 30 | Y |
| hMN3VH | | QVQLQ | 10 | P | 20 | L | 30 | Y |
| | | | | | | | | |
| EU_VH | 50 | 52 | 60 | 70 | | | | |
| MN3VH | | | | | | | | |
| hMN3VH | | | | | | | | |
| | | | | | | | | |
| EU_VH | 80 | 82 | 90 | 100 | 110 | | | |
| MN3VH | | | | | | | | |
| hMN3VH | | | | | | | | |
| | | | | | | | | |
| EU_VH | 103 | 110 | 113 | | | | | |
| MN3VH | | | | | | | | |
| hMN3VH | | | | | | | | |
| | | | | | | | | |

Figure 4B. Amino acid sequence alignment of EU (FR1-3) and KOL (FR4). MN3 and hMN3 heavy chain variable domains. Dots indicate the residues in MN3 is identical to the corresponding residues in RE1. Dashes represent gaps introduced to aid the alignment. Boxed represent the GDR regions. Both N- and C-terminal residues (underlined) of hMN3 are fixed by the staging vector used. Therefore, the corresponding terminal residues of MN3 are not compared with that of human VH sequences. Kabat's Ig molecule numbering scheme is used (same as in Fig. 1A).